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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,006	07/15/2003	Beverly L. Davidson	17023.013US2/01023	9111

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EXAMINER	
BLUMEL, BENJAMIN P	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/621,006	DAVIDSON ET AL.	
	Examiner	Art Unit	
	Benjamin P. Blumel	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *August 25, 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *3-13* is/are allowed.

6)☒ Claim(s) *1,2 and 14-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/15/2003 & 6/26/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of invention I drawn to claims 1-21 in the reply filed on August 25, 2006 is acknowledged. The traversal is on the ground(s) that examination of all the cells stated in claims 16-20 should be searched, given that such a search would not impose a burden on the Examiner. The examiner accepts the argument and will include the non-elected claims 16-19 in the present Office Action.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on July 15, 2003 and June 26, 2006 were filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Objections

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. The specification is objected to because the drawing descriptions do not indicate which SEQ ID NO: pertains to each amino acid sequence depicted in drawing 1.

The disclosure is objected to because of the following informalities: the U.S. Application Serial No. 09/758,008 incorporated by reference in the instant application was issued as a patent, US# 6,635,466, on October 21, 2003. Applicant is required to amend the specification addressing the present status of U.S. Application '008.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 14 and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Von Seggern et al. (USPGPub# 2003/0157688).

The instant invention is drawn to a method of transducing a CAR lacking cell with an adenovirus comprising a chimeric fiber polypeptide comprising a tail region, shaft region and knob region (required to infect target cells). In addition the adenovirus comprises a therapeutic agent encoded by the vector.

Von Seggern et al. teaches targeting specific cells and tissues with an adenovirus comprising a chimeric fiber protein of the tail and shaft region from Ad5 (of group C) and the knob/head region of Ad3 (of group B). The rationale behind developing a chimeric fiber polypeptide was provided by the ability of different subgroups of adenovirus to infect different cells more efficiently. Von Seggern et al. observed that the

chimeric adenovirus infected fibroblasts and monocytic cells more efficiently than wild type Ad5. Furthermore, Von Seggern et al. discusses utilizing such a vector to target specific cells and tissues with therapeutic agents, such as nucleotide sequences, which encode therapeutic polypeptides for treating tumors. For example, thymidine kinase can be expressed by the adenovirus vector in conjunction with granciclovir to inhibit DNA synthesis of the infected cell. Suicide genes or other enzymes and related metabolites can be included with the instant invention as part of a gene therapy regimen.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 14-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Von Seggern et al., Zabner et al. (Journal of Virology, 1999), and Chillon et al. (Journal of Virology, 1995).

The instant invention is drawn to a method of transducing a CAR lacking cell with an adenovirus comprising a chimeric fiber polypeptide comprising a tail region, shaft region and knob region with at least one of these regions from Ad30 (of group D). In addition the adenovirus comprises a therapeutic agent encoded for by the vector. The CAR lacking cell can be a neuronal, epithelial, tumor, neuroprogenitor or stem cell.

The teachings of Von Seggern et al., as stated above, are not drawn to utilizing an adenovirus with a chimeric fiber polypeptide comprised of a tail, shaft and/or knob region from Ad30.

Zabner et al. teaches enhanced genetic transfer with an adenovirus vector comprising a chimeric fiber polypeptide. Several wild-type adenoviruses from groups A-F, were compared in the ability to infect human epithelial cells. Wild-type Ad2 (group C) was 43 times less efficient than Ad17 (group D), also a wild type. Therefore, to examine if the fiber protein of Ad17 might enhance the infection rate of Ad2 Zabner et al. compared the ability of Ad2/βgal and Ad2/Ad17/βgal, a chimeric, to infect epithelial cells. The chimeric adenovirus transferred the βgal gene more efficiently resulting in a rate of 15-95 more βgal expression as compared to Ad2/βgal.

Chillon et al. teaches the different infection efficiencies of the multiple Adenovirus groups. Chillon et al. compared the ability of serotypes from groups A-F at infecting human umbilical vein endothelial cells (HUVEC) and central nervous system (CNS) cells. The following serotypes were used in the comparison: Ad31 of group A, Ad3, 7, and 14 of group B, Ad2 of group C, Ad9, 17, 19, 26 and 30 of group D, Ad4 of group E and Ad41 of group F. Following a 48-hour incubation period, post-infection, it was determined the adenovirus serotypes representing groups B and D had the highest rate of infection of HUVEC (20-60% and 20-90% respectively) and groups D and F infected CNS cells most efficiently (20-60% and 40% respectively). Of the least efficient serotypes to infect the target cells, Ad2 and 31 infected 5% of the CNS cells but did not infect HUVEC. The serotype able infect the highest percentage of both target cell types was Ad30, 60% for CNS cells and 90% for HUVEC. Chillon et al. further experimented with a chimeric fiber Adenovirus, testing the ability of ligating a portion of Ad17 fiber replacing most of the Ad2 fiber. A comparison was made between a chimeric

Ad2βgal2(17f) and Ad2βgal2 incubating with HUVEC and CNS cells. The later proved to be 21-fold and 7-fold less efficient at transferring the βgal gene.

It would have been obvious to one of ordinary skill in the art to modify the method taught by Von Seggern et al. in order to transduce a CAR lacking cell with an adenovirus vector that had chimeric fiber polypeptide with a region from Ad30, thereby enhancing the administration of a therapeutic agent to a targeted cell/tissue. One would have been motivated to do so, given the suggestion by Von Seggern et al. that the method be used to treat specific cells/tissues such as tumors with anti-tumor agents. There would have been a reasonable expectation of success, given the knowledge that forming a chimeric fiber comprising the knob, shaft and part of the tail from Ad17 and the remainder of the tail from Ad2 provided a more efficient transfer of genes to target cells as compared with Ad2-wild type, as taught by Zabner et al., and also given the knowledge that serotypes from groups B and D, particularly Ad30 and 17, offer a more efficient infectivity of HUVEC and CNS cells (cells lacking CAR), as taught by Chillon et al. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Summary

Allowable Subject Matter

The following is a statement of reasons for the indication of allowable subject matter: the sequences stated in claims 3-13 appear to be free of the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin P. Blumel whose telephone number is 571-272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Benjamin Blumel
Patent Examiner

BRUCE R. CAMPELL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Notice to Comply	Application No. 10/621,006	Applicant(s) Davidson et al.	
	Examiner Benjamin Blumel	Art Unit 1648	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: The disclosure is missing SEQ ID NO:s, see attached Action under Objections.

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☐ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☐ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
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